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**Abstract:** The pro-survival Bcl-I protein family are well known for their key roles in normal cellular function including the regulation of the intrinsic apoptotic pathway and general cell survival. Due to these central roles, family members like BCL2 and MCL1 are often deregulated in cancer, making them attractive targets for cancer therapeutics. However, family member Bfl-1 (Bcl-2-related protein AI) remains relatively understudied. This presentation will focus on efforts to identify potent and selective small molecule inhibitors starting from a DNA-encoded library (DEL) screening campaign. Leveraging structure-based drug design, application of a suite of predictive models and a robust assay cascade, a series of small molecule inhibitors were identified that potently and selectively disrupts the interaction of BH3 pro-apoptotic proteins with Bfl-1, both biochemically and cellularly. Optimization of these molecules further in a beyond-rule-of-five space then led to in vivo tools able to address key questions about this relatively lesser known BCL2 family member. Lessons learned from both this program and across a Discovery career including the importance of agility, the willingness to embrace uncertainty, and the ongoing benefit of learning from both challenges and achievements throughout will be shared.

**Bio:** Callie hails from South Carolina and earned her undergraduate degrees from Clemson University. She then pursued her PhD under the guidance of Professor Chi-Huey Wong at The Scripps Research Institute followed by an American Cancer Society postdoctoral fellowship at the California Institute of Technology. Since entering industry, her career has spanned positions in discovery chemistry at Amgen and Genentech, where she had the pleasure of working on a number of kinase inhibitor programs that achieved clinical validation. Ultimately, Callie returned to the east coast leading to her current role as a Scientific Director in Global Discovery Chemistry - Medicinal Chemistry at Johnson & Johnson, where she leads the peptide modality. On a more personal note, Callie enjoys engaging in lively debates about the merits of Carolina barbecue with her yankee colleagues and organizes an annual shrimp boil to share the delights of low country cuisine. Additionally, she is extremely honored to present as the Women in Chemistry lecturer as a proud girl mom which is equal parts thrilling and daunting, much like discovery.